

**ABSTRACT**

The use of mismatch repair (MMR) defective antibody producer cells offers a method to generate subclone variants with elevated protein production such as antibodies. Using MMR defective cells and animals, new cell lines and animal varieties with novel and useful properties such as enhanced protein production can be generated more efficiently than by relying on the natural rate of mutation. These methods are useful for generating genetic diversity within host cells to alter endogenous genes that can yield increased titer levels of protein production. By employing this method, two genes were discovered whose suppressed expression is associated with enhanced antibody production. Suppressed expression of these genes by a variety of methods leads to increased antibody production for manufacturing as well as strategies for modulating antibody production in immunological disorders. Moreover, the suppression of these two genes in host cells can be useful for generating universal high titer protein production lines.